IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Attorney Docket No. 06-132-A1)

Application of:	**Richard Martin et al.**	)	
		)	
Serial No.:	**To Be Assigned**	)	**Group Art Unit: TBA**
		)	
Int'l Serial No.:	**PCT/US04/037642**	)	**Examiner: TBA**
		)	
Filing Date:	**Herewith**	)	
		)	**Confirmation No.: TBA**
Title:	**Substituted Pyrimidine Compositions And Methods Of Use**	)	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Dear Sir:

Please consider the following amendments and remarks.

Amendments to the claims begin on page 2.

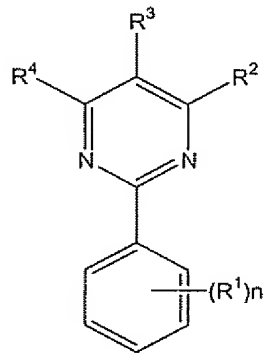
Remarks **begin on page** 17.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (original) A pharmaceutical composition comprising a compound of (I)



(I)

wherein

n is 0 to 5;

R^1 is each independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, hydroxycarbonyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, aminoalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R^2 and R^3 are selected as in a) or b) as below,

a) R^2 is selected from the group consisting of optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aralkyl, and optionally substituted heteroaralkyl, $-OR^6$, $-S(O)_tR^6$, $-N(R^7)R^8$, $-N(R^9)S(O)_tR^{10}$, $-C(O)R^6$, $-C(O)OR^6$, and $-C(O)N(R^7)R^8$; and R^3 is independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, aminoalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl; or

b) R^2 and R^3, together with the carbon atom to which they are attached, form an optionally substituted cycloalkyl ring, optionally substituted heterocyclyl ring, an optionally substituted cycloalkenyl ring;

R^4 selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl optionally substituted heterocyclylalkyl, $-R^{12}-OR^{13}$, $-R^{12}-N(R^{14})R^{15}$, $-R^{12}-C(O)R^{13}$, $-R^{12}-C(O)OR^{15}$, $-R^{12}-C(O)N(R^{14})R^{15}$, $-R^{12}-N(R^{14})C(O)R^{15}$, $-R^{12}-N(R^{14})C(O)OR^{15}$, $-R^{12}-S(O)_tR^{15}$ and $-R^{12}-S(O)_tN(R^{14})R^{15}$;

R^6 represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^7 represents H or optionally substituted alkyl;

R^8 represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^9 represents H or optionally substituted alkyl;

R^{10} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

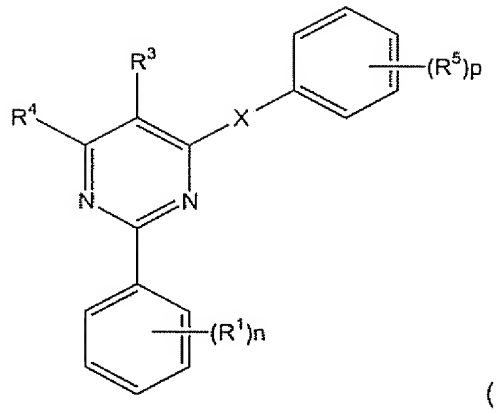
R^{12} represents a C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6alkynyl or C_1-C_6 alkoxy;

R^{13} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{14} represents H or optionally substituted alkyl;

R^{15} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl, and where each t is independently 0 to 2.

2. (original) The pharmaceutical composition of claim 1, wherein said compound has a formula (II)



(II)

wherein

n is 0 to 2; p is 0 to 2; X is $N(R^7)$,O, or $S(O)_r$ where r is 0 to 2;

R^1 is each independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, hydroxycarbonyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, aminoalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R^3 is independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, aminoalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl; or

R^4 selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl optionally substituted heterocyclylalkyl, $-R^{12}-OR^{13}$, $-R^{12}-N(R^{14})R^{15}$, $-R^{12}-C(O)R^{13}$, $-R^{12}-C(O)OR^{15}$, $-R^{12}-C(O)N(R^{14})R^{15}$, $-R^{12}-N(R^{14})C(O)R^{15}$, $-R^{12}-N(R^{14})C(O)OR^{15}$, $-R^{12}-S(O)_tR^{15}$ and $-R^{12}-S(O)_tN(R^{14})R^{15}$;

each R^5 independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, hydroxycarbonyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, $-OR^{20}$, $-S(O)_tR^{20}$, $-N(R^7)R^{20}$, $-N(R^9)S(O)_tR^{20}$, $-C(O)R^{20}$, and $-C(O)OR^{20}$;

R^7 and R^9 are each independently H or optionally substituted alkyl;

R^{12} represents a C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6alkynyl or C_1-C_6 alkoxy represents H or optionally substituted alkyl;

R^{13} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{14} represents H or optionally substituted alkyl;

R^{15} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{20} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl and where each t is independently 0 to 2.

3. (original) The pharmaceutical composition of claim 2 of formula (II) wherein;

n is 0; p is 0 to 2; X is $N(R^7)$, O, or $S(O)_r$ where r is 0 to 2;

R^3 is independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, aminoalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R^4 selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl optionally substituted heterocyclylalkyl, $-R^{12}-OR^{13}$, $-R^{12}-N(R^{14})R^{15}$, $-R^{12}-C(O)R^{13}$,$-R^{12}-C(O)OR^{15}$, $-R^{12}-C(O)N(R^{14})R^{15}$, $-R^{12}-N(R^{14})C(O)R^{15}$, $-R^{12}-N(R^{14})C(O)OR^{15}$, $-R^{12}-S(O)_tR^{15}$ and $-R^{12}-S(O)_tN(R^{14})R^{15}$;

each R^5 independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, hydroxycarbonyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, $-OR^{20}$, $-S(O)_tR^{20}$, $-N(R^7)R^{20}$, $-N(R^9)S(O)_tR^{20}$, $-C(O)R^{20}$, and $-C(O)OR^{20}$;

R^7 and R^9 are each independently H or optionally substituted alkyl; and

R^{12} represents a C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6alkynyl or C_1-C_6 alkoxy;

R^{13} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{14} represents H or optionally substituted alkyl;

R^{15} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl; and
R^{20} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl, and where each t is independently 0 to 2.

4. (original) The pharmaceutical composition of claim 2 of formula (II) wherein;
n is 0 to 2; p is 0 to 2; X is $N(R^7)$, O, or $S(O)_r$, where r is 0 to 2;
R^1 is each independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, hydroxycarbonyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, aminoalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;
R^3 is independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, lower alkoxy, and lower aminoalkyl;
R^4 selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl optionally substituted heterocyclylalkyl, $-R^{12}-OR^{13}$, $-R^{12}-N(R^{14})R^{15}$, $-R^{12}-C(O)R^{13}$ $-R^{12}-C(O)OR^{15}$, $-R^{12}-C(O)N(R^{14})R^{15}$, $-R^{12}-N(R^{14})C(O)R^{15}$, $-R^{12}-N(R^{14})C(O)OR^{15}$, $-R^{12}-S(O)_tR^{15}$ and $-R^{12}-S(O)_tN(R^{14})R^{15}$;
each R^5 independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, hydroxycarbonyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, $-OR^{20}$, $-S(O)_tR^{20}$, $-N(R^7)R^{20}$, $-N(R^9)S(O)_tR^{20}$, $-C(O)R^{20}$, and $-C(O)OR^{20}$;
R^7 and R^9 are each independently H or optionally substituted alkyl;
R^{12} represents a C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6alkynyl or C_1-C_6 alkoxy;
R^{13} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;
R^{14} represents H or optionally substituted alkyl;

R^{15} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{20} is represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl, and where each t is independently 0 to 2.

5. (original) The pharmaceutical composition of claim 2 of formula (II) wherein;

n is 0 to 2; p is 0 to 2; X is $N(R^7)$, O, or $S(O)_r$ where r is 0 to 2;

R^1 is each independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, hydroxycarbonyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, aminoalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R^3 is independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, aminoalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl; or

R^4 selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alky, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, $-R^{12}-OR^{13}$, $-R^{12}-N(R^{14})R^{15}$, $-R^{12}-C(O)R^{13}$ $-R^{12}-C(O)OR^{15}$, $-R^{12}-C(O)N(R^{14})R^{15}$, $-R^{12}-N(R^{14})C(O)R^{15}$, $-R^{12}-S(O)_tR^{15}$;

each R^5 independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, hydroxycarbonyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, $-OR^{20}$, $-S(O)_tR^{20}$, $-N(R^7)R^{20}$, $-N(R^9)S(O)_tR^{20}$, $-C(O)R^{20}$, and $-C(O)OR^{20}$;

R^7 and R^9 are each independently H or optionally substituted alkyl;

R^{12} represents a C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6alkynyl or C_1-C_6 alkoxy;

R^{13} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{14} represents H or optionally substituted alkyl;

R^{15} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{20} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl, and where each t is independently 0 to 2.

6. (original) The pharmaceutical composition of claim 2 of formula (II) wherein;
n is 0 to 2; p is 0 to 2; X is $N(R^7)$, O, or $S(O)_r$ where r is 0 to 2;

R^1 is each independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, hydroxycarbonyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, aminoalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl;

R^3 is independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, aminoalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocyclyl; or

R^4 selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heterocyclyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl optionally substituted heterocyclylalkyl, $-R^{12}-OR^{13}$, $-R^{12}-N(R^{14})R^{15}$, $-R^{12}-C(O)R^{13}$, $-R^{12}-C(O)OR^{15}$, $-R^{12}-C(O)N(R^{14})R^{15}$, $-R^{12}-N(R^{14})C(O)R^{15}$, $-R^{12}-N(R^{14})C(O)OR^{15}$, $-R^{12}-S(O)_tR^{15}$ and $-R^{12}-S(O)_tN(R^{14})R^{15}$;

each R^5 independently selected from the group consisting of halo, cyano, nitro, hydroxyl, formyl, hydroxycarbonyl, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, $-OR^{20}$, $-S(O)_tR^{20}$, $-N(R^7)R^{20}$, $-C(O)R^{20}$, and $-C(O)OR^{20}$;

R^7 and R^9 are each independently H or optionally substituted alkyl;

R^{12} represents a C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6alkynyl or C_1-C_6 alkoxy;

R^{13} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{14} represents H or optionally substituted alkyl;

R^{15} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl and

R^{20} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl, and where each t is independently 0 to 2.

7. (original) The pharmaceutical composition of claim 2 of formula (II) wherein;

n is 0 or 1; p is 1 to 2; X is $N(R^7)$;

R^1 is each independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, hydroxycarbonyl, optionally substituted alkyl, alkoxy, and aminoalkyl;

R^3 is independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, lower alkoxy, and lower aminoalkyl;

R^4 selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alky, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, $-R^{12}-OR^{13}$, $-R^{12}-N(R^{14})R^{15}$, $-R^{12}-C(O)R^{13}$, $-R^{12}-C(O)OR^{15}$, $-R^{12}-C(O)N(R^{14})R^{15}$, $-R^{12}-N(R^{14})C(O)R^{15}$, $-R^{12}-S(O)_tR^{15}$;

each R^5 independently selected from the group consisting of halo, cyano, nitro, hydroxyl, formyl, hydroxycarbonyl, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, $-OR^{20}$, $-S(O)_tR^{20}$, $-N(R^7)R^{20}$, $-C(O)R^{20}$, and $-C(O)OR^{20}$;

R^7 and R^9 are each independently H or optionally substituted alkyl;

R^{12} represents a C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6alkynyl or C_1-C_6 alkoxy;

R^{13} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{14} represents H or optionally substituted alkyl;

R^{15} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{20} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl, and where each t is independently 0 to 2.

8 (original) The pharmaceutical composition of claim 2 of formula (II) wherein;

n is 0 or 1; p is 1 to 2; X is $S(O)_r$, where r is 0;

R^1 is each independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, hydroxycarbonyl, optionally substituted alkyl, alkoxy, and aminoalkyl;

R^3 is independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, lower alkoxy, lower aminoalkyl;

R^4 selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alky, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, $-R^{12}-OR^{13}$, $-R^{12}-N(R^{14})R^{15}$, $-R^{12}-C(O)R^{13}$, $-R^{12}-C(O)OR^{15}$, $-R^{12}-C(O)N(R^{14})R^{15}$, $-R^{12}-N(R^{14})C(O)R^{15}$, $-R^{12}-S(O)_tR^{15}$;

each R^5 independently selected from the group consisting of halo, cyano, nitro, hydroxyl, formyl, hydroxycarbonyl, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, $-OR^{20}$, $-S(O)_tR^{20}$, $-N(R^7)R^{20}$, $-C(O)R^{20}$, and $-C(O)OR^{20}$;

R^7 and R^9 are each independently H or optionally substituted alkyl;

R^{12} represents a C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6alkynyl or C_1-C_6 alkoxy;

R^{13} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{14} represents H or optionally substituted alkyl;

R^{15} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{20} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl, and where each t is independently 0 to 2.

9. (original) The pharmaceutical composition of claim 2 of formula (II) wherein;

n is 0 or 1; p is 1 to 2; X is O;

R^1 is each independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, hydroxycarbonyl, optionally substituted alkyl, alkoxy, and aminoalkyl;

R^3 is independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, alkoxy, and lower aminoalkyl;

R^4 selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alky, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, $-R^{12}-OR^{13}$, $-R^{12}-N(R^{14})R^{15}$, $-R^{12}-C(O)R^{13}$, $-R^{12}-C(O)OR^{15}$, $-R^{12}-C(O)N(R^{14})R^{15}$, $-R^{12}-N(R^{14})C(O)R^{15}$, and $-R^{12}-S(O)_tR^{15}$;

each R^5 independently selected from the group consisting of halo, cyano, nitro, hydroxyl, formyl, hydroxycarbonyl, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, $-OR^{20}$,$-S(O)_tR^{20}$, $-N(R^7)R^{20}$, $-C(O)R^{20}$, and $-C(O)OR^{20}$;

R^7 and R^9 are each independently H or optionally substituted alkyl;

R^{12} represents a C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6alkynyl or C_1-C_6 alkoxy;

R^{13} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{14} represents H or optionally substituted alkyl;

R^{15} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl and

R^{20} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl, and where each t is independently 0 to 2.

10. (original) The pharmaceutical composition of claim 2 of formula (II) wherein;

n is 0 or 1; p is 1 to 2; X is $S(O)_r$ where r is 2;

R^1 is each independently selected from the group consisting of halo, pseudohalo, cyano, nitro, hydroxyl, hydroxycarbonyl, optionally substituted alkyl, alkoxy, and aminoalkyl;

R^3 is independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, lower alkoxy, and lower aminoalkyl;

R^4 selected from the group consisting of hydrogen, halo, pseudohalo, cyano, nitro, hydroxyl, formyl, mercapto, optionally substituted alky, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, $-R^{12}-OR^{13}$, $-R^{12}-N(R^{14})R^{15}$, $-R^{12}-C(O)R^{13}$, $-R^{12}-C(O)OR^{15}$, $-R^{12}-C(O)N(R^{14})R^{15}$, $-R^{12}-N(R^{14})C(O)R^{15}$, $-R^{12}-S(O)_tR^{15}$;

each R^5 independently selected from the group consisting of halo, cyano, nitro, hydroxyl, formyl, hydroxycarbonyl, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, $-OR^{20}$, $-S(O)_tR^{20}$, $-N(R^7)R^{20}$, $-C(O)R^{20}$, and $-C(O)OR^{20}$;

R^7 and R^9 are each independently H or optionally substituted alkyl;

R^{12} represents a C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6alkynyl or C_1-C_6 alkoxy;

R^{13} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{14} represents H or optionally substituted alkyl;

R^{15} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl;

R^{20} represents optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl or optionally substituted heterocyclyl, and where each t is independently 0 to 2.

11. (currently amended) The pharmaceutical composition of ~~any of claims 1-10~~claim 1 wherein each t is independently 0 or 2.

12. (currently amended) The pharmaceutical composition of ~~any of claims 1-11~~claim 1 wherein the substituents, when substituted, are independently substituted with a group selected from Q^1, wherein Q^1 represents alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cyano, nitro, halo, hydroxyl, hydroxycarbonyl, pseudohalo, $-R^{30}-OR^{31}$, $-R^{30}-SR^{16}$, $-R^{30}-N(R^{32})(R^{33})$, $-R^{30}-C(J)R^{34}$, $-R^{30}-C(J)OR^{31}$, $-R^{30}-C(J)N(R^{32})(R^{33})$, $-R^{30}-C(J)N(R^{31})N(R^{32})(R^{33})$, $-R^{30}-N(R^{31})C(J)R^{34}$, $-R^{30}-N(R^{31})C(J)OR^{31}$, $-R^{30}-N(R^{31})C(J)N(R^{32})(R^{33})$, $-R^{30}-OC(J)R^{34}$, $-R^{30}-OC(J)OR^{31}$, $-R^{30}-OC(J)N(R^{32})(R^{33})$, $-Si(R^{35})_3$, $-N(R^{31})S(O)_yR^{36}$ or $-R^{30}-S(O)_yR^{36}$;

where each R^{30} is independently a direct bond or a straight or branched alkylene chain;

R^{31} and R^{34} are each independently hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoalkenyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl or heteroaralkyl;

R^{32} and R^{33} are each independently hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoalkenyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl or heteroaralkyl;

or R^{32} and R^{33} together with the nitrogen atom to which they are attached, form a heterocyclyl, heterocyclylalkenyl, or heteroaryl;
R^{35} R^{36} and R^{16} are each independently alkyl, alkenyl, alkynyl, haloalkyl, alkoalkenyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl or heteroaralkyl;
each J is independently O or S; and each y is independently 0 to 2.

13. (currently amended) The pharmaceutical composition of ~~any of claims 1-11~~ claim 1 wherein the substituents, when substituted, are independently substituted with a group selected from Q^1, wherein Q^1 represents alkyl, alkoxy, aminoalkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cyano, nitro, halo, hydroxyl, hydroxycarbonyl or pseudohalo.

14. (original) A pharmaceutical composition comprising a compound selected from FIG. 1.

15. (currently amended) A method of altering the activity of a NGFI-B family member, or heterodimeric complex thereof by contacting said NGFI-B family member, or heterodimeric complex thereof with a compound or composition of ~~claims 1-14~~claim 1.

16. (original) The method of claim 15, wherein said NGFI-B family member is NGFI-Bβ, and said heterodimeric complex comprises NGFIBβ and RXR.

17. (currently amended) A method for the treatment, prevention, or amelioration of one or more symptoms of a disease or disorder that is modulated by NGFI-B family activity, or in which NGFI-B family activity is implicated comprising administering any compound or composition of ~~claims 1-14~~claim 1 to a patient in need of such treatment.

18. (original) The method of claim 17, wherein said NGFI-B family activity is NGFI-B β or NGFIBβ / RXR heterodimer activity.

19. (original) The method of claim 17, wherein said disease or disorder is selected from Parkinson's disease, cancer, Alzheimer's disease, schizophrenia, manic depressive illness, multiple sclerosis, neuronal inflammatory responses, neuronal injury, stroke, neuronal degeneration, inflammation, acute inflammatory reactions, osteoporosis, arthritis, rheumatoid arthritis, psoriatic arthritis, sarcoid arthritis, osteoarthritis, ulcerative colitis, thyrroiditis, atherosclerosis, and atherosclosis related cardiovascular and coronary heart

disease by administering a compound or composition of the present invention to patient in need of such treatment.

20. (currently amended) A method for regulating the activity of NGFI-B β / RXR heterodimers in neuronal cells in culture, comprising incubating a stem cell with any compound or composition of ~~claims 1-14~~claim 1.

21. (original) The method of claim 20, wherein said stem cell is an embryonic stem cell.

22. (original) The method of claim 20, wherein said stem cell is derived from an adult.

23. (currently amended) A method for maintaining neuronal cell viability after a transplantation procedure comprising administering to a donor recipient ~~any of the compounds or compositions of claims 1-14~~the compound or composition of claim 1.

24. (currently amended) A method for the treatment, prevention, or amelioration of Parkinson's disease comprising administering to a patient in need thereof of ~~one of the compounds or compositions of claims 1-14~~the compound or composition of claim 1.

25. (currently amended) A method for the treatment, prevention, or amelioration of Alzheimer's disease comprising administering to a patient in need thereof of ~~one of the compounds or compositions of claims 1-14~~the compound or composition of claim 1.

26. (currently amended) A method for the treatment, prevention, or amelioration of multiple sclerosis comprising administering to a patient in need thereof of ~~one of the compounds or compositions of claims 1-14~~the compound or composition of claim 1.

27. (currently amended) A method for the treatment, or prevention of an inflammatory immune disease in a subject by administering to the subject in need of such treatment ~~any one of the compounds or compositions of claims 1-14~~ the compound or composition of claim 1.

28. (original) The method of claim 27, wherein said inflammatory disease is selected from arthritis, rheumatoid arthritis (RA); psoriatic arthritis, infectious arthritis, juvenile rheumatoid arthritis; osteoarthritis, and spondyloarthropaties.

29. (currently amended) A method for the treatment, prevention, or amelioration of a coronary heart disease event, a cerebrovascular event, and /or intermittent claudication in a subject by administering to the subject in need of such treatment ~~any one of the compounds or compositions of claims 1-14~~the compound or composition of claim 1.

30. (currently amended) A method for the treatment, prevention, or amelioration of osteoporosis in a subject by administering to the subject in need of such treatment ~~any one of the compounds or compositions of claims 1-14~~ the compound or composition of claim 1.

31. (currently amended) A pharmaceutical composition comprising ~~any one of the compounds or compositions of claims 1-14~~ the compound or composition of claim 1 and an additional active compound.

32. (original) The pharmaceutical composition of claim 31, wherein said additional active compound is selected from levodopa (L-DOPA or L-dihydroxyphenylalanine), L-aromatic amino acid decarboxylase (AADC) inhibitors and catechol O-methyl transferase (COMT) inhibitors.

33. (original) The pharmaceutical composition of claim 31, wherein said additional active compound is selected from an anti-inflammatory compound.

34. (original) The pharmaceutical composition of claim 33, wherein said anti-inflammatory compound is selected from a matrix metalloproteinase inhibitor, an inhibitor of pro-inflammatory cytokines (e.g., anti-TNF molecules, TNF soluble receptors), non-steroidal anti-inflammatory drugs (NSAIDs), prostaglandin synthase inhibitors (e.g., choline magnesium salicylate, salicylsalicyclic acid), COX-1 or COX-2 inhibitors, (e.g. aspirin, acetaminophen, ibuprofen) or corticosteroids, (e.g. methylprednisone, prednisone, or cortisone).

35. (original) The pharmaceutical composition of claim 31, wherein said additional active compound is selected from an antihyperlipidemic agent; a plasma HDL-raising agent; an antihypercholesterolemic agent, such as a cholesterol biosynthesis inhibitor, e.g., an hydroxymethylglutaryl (HMG) CoA reductase inhibitor (also referred to as statins, such as lovastatin, simvastatin, pravastatin, fluvastatin, and atorvastatin), an HMG-CoA synthase inhibitor, a squalene epoxidase inhibitor, or a squalene synthetase inhibitor (also known as squalene synthase inhibitor); an acyl-coenzyme A cholesterol acyltransferase (ACAT) inhibitor, such as melinamide; probucol; nicotinic acid and the salts thereof and

niacinamide; a cholesterol absorption inhibitor, such as β-sitosterol; a bile acid sequestrant anion exchange resin, such as cholestyramine, colestipol or dialkylaminoalkyl derivatives of a cross-linked dextran; an LDL (low density lipoprotein) receptor inducer; fibrates, such as clofibrate, bezafibrate, fenofibrate, and gemfibrizol; vitamin B_6 (also known as pyridoxine) and the pharmaceutically acceptable salts thereof, such as the HCl salt; vitamin B_{12} (also known as cyanocobalamin); vitamin B_3 (also known as nicotinic acid and niacinamide, supra); anti-oxidant vitamins, such as vitamin C and E and beta carotene; a beta-blocker; LXR α or β agonists, antagonists, or partial agonists, FXR agonists, antagonists, or partial agonists, an angiotensin II antagonist; an angiotensin converting enzyme inhibitor; and a platelet aggregation inhibitor, such as fibrinogen receptor antagonists (i.e., glycoprotein IIb/IIIa fibrinogen receptor antagonists) and aspirin.

36. (original) The pharmaceutical composition of claim 31, wherein said additional active compound comprises parathyroid hormone (PTH) or physiologically active fragment thereof.

REMARKS

The claims of this U.S. national phase of a PCT application were amended to reduce the number of claims and remove multiple dependencies in order to reduce the filing fee. No new subject matter has been added, nor has the scope of the claims been amended.

Enclosed herewith is the ISR and Form SB/08a listing the art cited in the ISR. We understand copies of the art cited in the ISR will be forwarded to the PTO by the International Authorities.

If there are any questions or comments regarding this Preliminary Amendment or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

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/Michael S. Greenfield/
Michael S. Greenfield
Registration No. 37,142

McDonnell Boehnen Hulbert & Berghoff LLP
300 South Wacker Drive
Chicago, IL 60606
Telephone: 312-913-0001
Facsimile: 312-913-0002